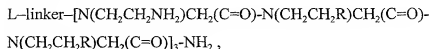


ABSTRACT

Chimeric oligonucleotide of the formula 5'-W-X¹-Y-X²-Z-3', where W represents a 5'-O-alkyl nucleotide, each of X¹ and X² represents a block of seven to twelve phosphodiester-linked 2'-O-alkyl ribonucleotides, Y represents a block of five to twelve phosphorothioate-linked deoxyribonucleotides, and Z represents a blocking group effective to block nuclease activity at the 3' end of the oligonucleotide, are described. These compounds exhibit high resistance to endo- and exonucleases, high sequence specificity, and the ability to activate RNase H, as evidenced by efficient and long-lasting suppression of target mRNA. The oligonucleotides are preferably transfected into cells in formulations containing a lipid-peptoid conjugate carrier molecule of the formula



where L is a lipid moiety, including a steroid, and each group R is independently selected from alkyl, aminoalkyl, and aralkyl.